1997); and *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 122 S.Ct. 1831 2002 WL 1050479 U.S..

Amendments Entered

Applicants note that an amendment filed 02/08/2002 had been entered and thank the examiner.

Non-statutory Double Patenting

The Examiner has maintained the provisional obviousness-type double patenting rejection of claims 5-8 and 10-22, over claims 1-17, 24-43, and 50-69 of copending Application Ser. No. 09/285,658. See, paper No. 17 at pages 2-3, paragraph 3. Applicants respectfully traverse this rejection. Without acquiescing to the rejections, and because these rejections are provisional, Applicants respectfully request that the rejections be held in abeyance until a patent may issue from copending Application Ser. No. 09/285,658.

Withdrawn Rejections

Applicants acknowledge and thank the Examiner for withdrawing the rejection of claims 1, 3-13, and 20-25 under 35 U.S.C. §112, second paragraph because of the previous amendment.

Anticipation Rejection Under 35 U.S.C. §102(b)

The Examiner rejected claims 1, 3-7 and 22-25 under 35 U.S.C. §102(b) over Sooknanan *et. al.* (WO96/17079). See paper No. 17 at page 7, paragraph 4. Applicants respectfully traverse this rejection.

As claimed, the current invention relates to a method for amplification of a population of different types of nucleic acids wherein a four-enzyme mix comprising a DNA Polymerase is used to synthesize double-stranded DNA from a population of single-stranded DNA.

Sooknanan *et. al.* teaches a method for amplifying one specific nucleic acid sequence or its complement and requires the presence of a terminal repeat in the template. Sooknanan *et. al.* does not teach or disclose the amplification of a nucleic acid population of different types as the current invention does and in fact, it teaches away from the amplification of a population of different types of nucleic acids, such as total cellular RNA, because the method requires all sequences to be amplified to have a

terminal repeat. A specific nucleic acid refers to a targeted or particular sequence of nucleic acid whereas a population of nucleic acid refers to a group of nucleic acids of the same species relatively isolated from other groups of the same species. Sooknanan *et. al.* teaches that the 5' –terminal sequence and the 3' –terminal sequence are self-complementary and serves as terminal repeats whereas in our invention, there is no limitation of the 5' and the 3' ends being self-complementary or serving as terminal repeats. Consequently, Applicants assert that Sooknanan *et. al.* does not show or suggest the presently claimed invention as Sooknanan *et. al.* does not amplify a population of nucleic acids as specified in claim 1 and therefore, this rejection should be withdrawn.

The Examiner argues that there is no limitation in the claim language on what is the temperature range for the thermal stable polymerase. However, claim 26 which describes thermo-stable enzyme depends from independent claim 1 which should patentable because of the arguments listed above.

Obviousness Rejection Under 35 U.S.C. §103(a)-Sooknanan et. al. in view of Kwoh et. al. and Goller et. al.

The Examiner has rejected claims 8-13 under 35 U.S.C. 103(a) over Sooknanan *et al.* as applied to claims 1 and 3-7 of the instant claims, and further in view of Kwoh *et. al.* and Goller *et. al.*. Applicants respectfully traverse this rejection.

For the reasons listed above, Sooknanan *et. al.* fails to teach all of the limitations of claim 1. Kwoh *et. al.* and Goller *et. al.* do not remedy the deficiencies of Sooknanan *et. al.*. Like Sooknanan *et. al.*, Kwoh *et. al.* teaches the amplification of one specific segment or fragment of a nucleic acid sequence of interest whereas the present claims cover a population of nucleic acid sequences of different types. Additionally, Goller *et. al.* does not discuss targeting a population of nucleic sequences of different types and therefore, Goller *et. al.* does not show or suggest the presently claimed invention as Goller *et. al.* does not amplify a population of nucleic acids as suggested in claim 1.

Kwoh *et. al.* must be performed in a different tube because some of the reactions and buffers in Kwoh *et. al.* may not function effectively if they are conducted in the same tube. Additionally, Kwoh *et. al.* may lose some material when transferring to different tubes. In contrast, the present claims are limited to one tube; one benefit to use the same tube in order to save as much material as possible and to save time.

Goller *et. al.* teaches a method for identification of differentially expressed mRNA that requires purification of the double-stranded cDNA followed by directional cloning into a vector before RNA synthesis. Goller *et. al.* does not teach the amplification of a population of nucleic acid of different types and fails to teach the addition of the four enzyme mix whereas the current invention does teach the four enzyme mix. Finally, Goller *et. al.* teaches that the reactions occur in separate tubes whereas in the current invention the reactions occur in the same tube. Goller *et. al.* will not be effective in the same tube because the different buffer conditions of the invention only permit it to work in separate tubes. Contrary to Goller *et. al.*, the current invention allows the reactions to be performed in a single tube to save time and reaction material. Moreover, one in the ordinary skill in the art at the time would not combine Goller *et. al.* and Kwoh *et. al.* to apply nucleic acid isolated from eukaryotic cells or tissue with Sooknanan *et. al.* There is no suggestion or motivation, in Goller *et. al.*, Kwoh *et. al.*, or Sooknanan *et. al.* references or in the knowledge generally available to one of ordinary skill in the art to combine these references because neither of the references discuss amplification of a general population of nucleic acids as specified in claim 1.

Obviousness Rejection Under 35 U.S.C. §103(a)-Sooknanan et. al. in view of Schnipelsky et. al.

Claims 20-21 were rejected under 35 U.S.C. §103(a) over Sooknanan *et. al.* as applied to claims 1 and 3-7 above and further in view of Schnipelsky *et. al.*(5,229,297). See, paper No. 17 at page 7, paragraph 10. Applicants respectfully traverse this rejection.

For the reasons indicated above, Sooknanan *et. al.* fails to teach all of the limitations of claim 1 and Schnipelsky *et. al.* fails to remedy the deficiencies of Sooknanan *et. al.* as applied to dependent claims 20-21. The primary purpose of Schnipelsky *et. al.* is to prevent nucleic acid amplified by PCR technology from being released to the atmosphere. Schnipelsky *et. al.* makes no reference to a population of nucleic acid of different types. Additionally, there is no suggestion or motivation to apply this method, either in the references or knowledge generally available to one of ordinary skill in the art, to that of Sooknanan *et. al.* Furthermore, there is no reference in the

Sooknanan *et. al.* of any problem with the presence of nucleic acid inside the amplification device.

For these reasons and the reasons set forth *supra*, Applicants respectfully request that the rejection of claims under 35 U.S.C. §103(a) be reconsidered and withdrawn.

CONCLUSION

For these reasons, Applicants believe all pending claims are now in condition for allowance and should be passed to issue. If the Examiner feels that a telephone conference would in any way expedite the prosecution of the application, please do not hesitate to call the undersigned at (408) 731-5021.

The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account 01-0431.

If the Examiner has any questions pertaining to this application, the Examiner is requested to contact the undersigned attorney.

Respectfully submitted,

Date: July 23, 2002

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VERSION WITH MARKINGS TO SHOW CHANGES MADE TO THE APPLICATION

In the Claims

Please amend Claim 1 as follows:

1. (twice amended) A method for the amplification of a population of different types of nucleic acids in a single reaction vessel, said method comprising:

forming a population of different types of at least two or more distinct species of DNA/RNA hybrids from a population of different types of different single-stranded mRNA species;

forming a population of different types of single-stranded DNA from DNA/RNA hybrids;

synthesizing a population of different types of double-stranded DNA from a said single-stranded DNA population wherein a four enzyme-mix comprising at least a DNA polymerase is added to synthesize said double-stranded cDNA; and

producing multiple copies of RNA from said double-stranded DNA, wherein said DNA synthesis and RNA amplification steps occur in a single reaction vessel containing one or more reagents, where the reagents may contain an enzyme or enzyme mix.